REMARKS

Reconsideration is requested.

Claims 1-3, 5, 6, 9-11, 13-16 and 49-51are pending. The allowance of claims 11 and 13-15 is acknowledged, with appreciation.

The Section 103 rejection of claims 1-3, 5-6, 9-10, 16 and 49-51 over the combination of Seddon et al. (U.S. Patent 5,491,220), Hanai et al. (U.S. Patent 5,952,472) and Owen et al. (Journal of lrnmunological Methods, 1994, 168: 149-165), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

The Examiner states that the

> "instant claims are directed to a method of treating arthritis comprising administering an anti-FGF-8 antibody to inhibit activity of FGR-8, wherein the antibody is a monoclonal, humanized, i.e., human chimeric or human CDR-grafted, or a fragment thereof." See page 3 of the Office Action dated June 10, 2009.

Claims 1 and 49-51 however do not further define the antibody of the claim in the manner asserted by the Examiner. Moreover, claims 49-51 define methods of inhibiting joint destruction, protecting cartilage, and inhibiting growth of synovial membrane, respectively.

The Examiner states that although Seddon et al did not teach FGF-8 as the specific FGF to target for treating arthritis, given the finite known species of FGF, it allegedly would have been obvious to one of ordinary skill in the art to have targeted FGF-8.

Specifically, the Examiner asserts that

> The rational to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options (e.g., administration an anti-FGF-8 antibody for the therapeutic purposes as taught by Hanai et al.) within his or her technical grasp. This leads to the anticipated success of treating arthritis with inhibitory anti-FGF-8 antibody. It is likely the product not of innovation but of ordinary skill and common sense.
> Given that anti-FGF-8 antibody was a known inhibitor of FGF-8 as taught by Hanai et al, it would have been within the ordinary artisan's technical grasp to use Hanai's the antibody [sic] as an inhibitor of FGF-8 to treat arthritis as taught by Seddon et al.

The applicants respectfully disagree with the Examiner's assertions as Seddon et al specifically disclose FGF-2 analogues of which a part of sequence is replaced with a part of other cytokines or other FGF family and these FGF-2 analogues have similar secondary and tertiary structure of native FGF-2 and have desirable physiological properties such as FGF agonists or potential antagonists. Seddon et al explain their disclosure as follows at column 6, lines 7-15 of the patent (emphasis added):

> This invention is based upon the finding that changes in fibroblast growth factor surface loop residues in a manner that does not perturb the overall secondary and tertiary structure of the FGF molecule yields an array of structural analogues having varied and desirable physiological properties, including FGF agonists and potential antagonists. Changes in loop sequences, or sequences adjacent to loop sequences, yield analogues that bind to heparin and exhibit binding affinity to a native fibroblast growth factor receptor.

Seddon et al also produce FGF-2 analogues such as FGF-2LA, FGF-2LI which have weaker angiogenesis activity than that of native FGF-2 *in vitro* (see Fig. 6 of the patent) and have comparable or litter higher angiogenesis activity of native FGF-2 *in vivo* (see Fig. 8 of the patent). However, Seddon et al do not produce FGF-2 analogues

comprising potential inhibitory activity of physiological activity via FGF receptor, although FGF-2 analogues can inhibit native FGF-2 to bind to FGF receptor (see Fig. 9A of the patent).

On the basis of embodiments and descriptions disclosed in the specification, angiogenesis activity by FGFs were known to the ordinarily skilled person (see, last paragraph, column 1 of the patent). The following passage of Seddon et al (column 12, lines 42-49) however, either alone or in combination with the remaining cited art, would not have made the claimed invention obvious:

> FGF antagonists exhibiting reduced biological activity are useful as anticancer and antiproliferative agents. The antagonists that act as angiogenesis inhibitors are useful for the treatment of diseases where neovascularization is dominant in the pathology such as retinopathies of the eye, neovascular glaucoma, skin disorders, chronic inflammation, rheumatoid arthritis, and the like.

The applicants submit, for example, that there are many diseases where neovascularization is dominant in the pathology and the FGF family is known to contain many members (i.e., FGF1 to 9 molecules). Seddon et al fail to teach FGF-8 as the specific FGF to target for treating arthritis as the Examiner appears to suggest. Therefore, the applicants submit that the ordinarily skilled person would not have reasonably predicted which FGF molecule could be attributable to which neovascularization-dominant disease, to have made the claimed invention obvious. The applicants also believe that Seddon et al also fail to disclose any other antagonist such as an anti-FGF-8 neutralizing antibody.

Furthermore, although Hanai et al exactly disclose anti-FGF-8 antibody comprising neutralizing activity of biological activity of FGF-8, Hanai et al fail to disclose or suggest a method of treatment of arthritis patients which includes administering an anti-FGF-8 antibody. Accordingly, the applicants believe that one of ordinary skill in the art would not have predicted from the cited combination of art whether an anti-FGF-8 antibody would be useful for treating arthritis.

The applicants submit that there was no motivation in the cited art to have used an anti-FGF-8 antibody for treating arthritis. Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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